Journal of Cardiology Cases 11 (2015) 52–55

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

A Churg–Strauss syndrome patient with myopericardial involvement

Eva D. Papadimitraki (MD, PhD)[a,*], Ioannis Moyssakis (MD, PhD)[a], Sophie Mavrogeni (MD, PhD)[b], Maria Mylona (MD)[c], Dimitrios Anagnostou (MD)[a], Konstantinos Merkouris (MD)[a], John Barbetseas (MD, PhD)[a]

[a] Department of Cardiology, Laiko General Hospital, Athens, Greece
[b] Onassis Cardiac Surgery Center, Athens, Greece
[c] Department of Internal Medicine, Laiko General Hospital, University of Athens, Greece

ARTICLE INFO

Article history:
Received 25 July 2014
Received in revised form 6 October 2014
Accepted 10 October 2014

Keywords:
Churg–Strauss syndrome
Eosinophilic syndromes
Myopericarditis
Cardiac magnetic resonance
Heart disease in vasculitic syndromes

ABSTRACT

Churg–Strauss syndrome is a necrotizing vasculitis of small vessels characterized by upper and lower airway disease followed by peripheral eosinophilia and multiple organ involvement. Herein we present the case of a 45-year-old female patient with Churg–Strauss syndrome and myopericardial disease who improved upon cyclophosphamide treatment. Apart from discussing the characteristics of myopericardial disease in eosinophilic syndromes, we highlight the crucial role of cardiac imaging in the prompt recognition and management of such patients.

<**Learning objective:** Churg–Strauss syndrome is a vasculitic disorder characterized by massive hypereosinophilia and multi-organ disease. Myocardial involvement may manifest as myopericarditis, valvular dysfunction, myocardial infarction, or left ventricular thrombi or alternatively may only cause subclinical changes difficult to diagnose with conventional echocardiography. Cardiac magnetic resonance imaging is the gold-standard for the detection of active inflammation and fibrosis that may characterize myocardial disease. This is of major importance since timely diagnosis may enable the establishment of appropriate treatments and arrhythmia screening.>

Introduction

Churg–Strauss syndrome (CSS) is a rare necrotizing vasculitis of small vessels. Late onset asthma, nasal polyps, and sinusitis are early manifestations with eosinophilia and vasculitic tissue affecting nervous system, gastrointestinal tract, skin, and lungs, with heart involvement occurring later in the disease course.

Case report

Herein we present the case of a 45-year-old woman with CSS and history of asthma and nasal polyps, who presented with dyspnea (New York Heart Association III) of recent onset. On admission, the patient was in respiratory distress with blood pressure 110/70 mmHg and inspiratory crackles. Her chest-X-ray revealed bilateral pleural effusions and the electrocardiogram showed sinus tachycardia of 100 bpm, left ventricular hypertrophy, and diffuse horizontal ST segment depression. Blood analysis was remarkable for severe eosinophilia (15,000/μl), white blood cells 24,000/μl, abnormal troponin (1.5 ng/ml), and B-type natriuretic peptide 800 pg/ml.

Initial transthoracic echocardiogram (TTE) revealed a left ventricle (LV) of normal internal dimensions with mild systolic dysfunction (ejection fraction = 45%), hypokinetic inferior and inferolateral and mid/apical anteroseptal segments. There was marked hyperechogenicity of inferior and inferolateral wall involving both the subendocardial and subepicardial segments. An accompanying moderate pericardial effusion causing protodiastolic compression of the right ventricle was present. Mitral and tricuspid annular infiltrations with moderate valvular regurgitation were evident as well. Right ventricular hypertrophy with reduced tricuspid annular systolic velocity (7 cm/sec) was also found. There were no intraventricular thrombi. Interestingly, both global longitudinal and circumferential LV strain were severely impaired (−12% and −8%, respectively) (Fig. 1a, c and e).

The patient received cyclophosphamide (CYC) monthly doses of 2 g for six consecutive months and steroids (1 g methylprednisolone/24 h × 3 days switched to prednisolone with progressive tapering) with clinical improvement soon after the first infusion.

* Corresponding author at: Department of Cardiology, Laiko General Hospital, 17 Agiou Thoma Street, 11527 Goudi, Athens, Greece. Tel.: +30 2107456258; fax: +30 2132061761.
E-mail address: evapapadimitraki@hotmail.com (E.D. Papadimitraki).

http://dx.doi.org/10.1016/j.jccase.2014.10.003
1878-5409/

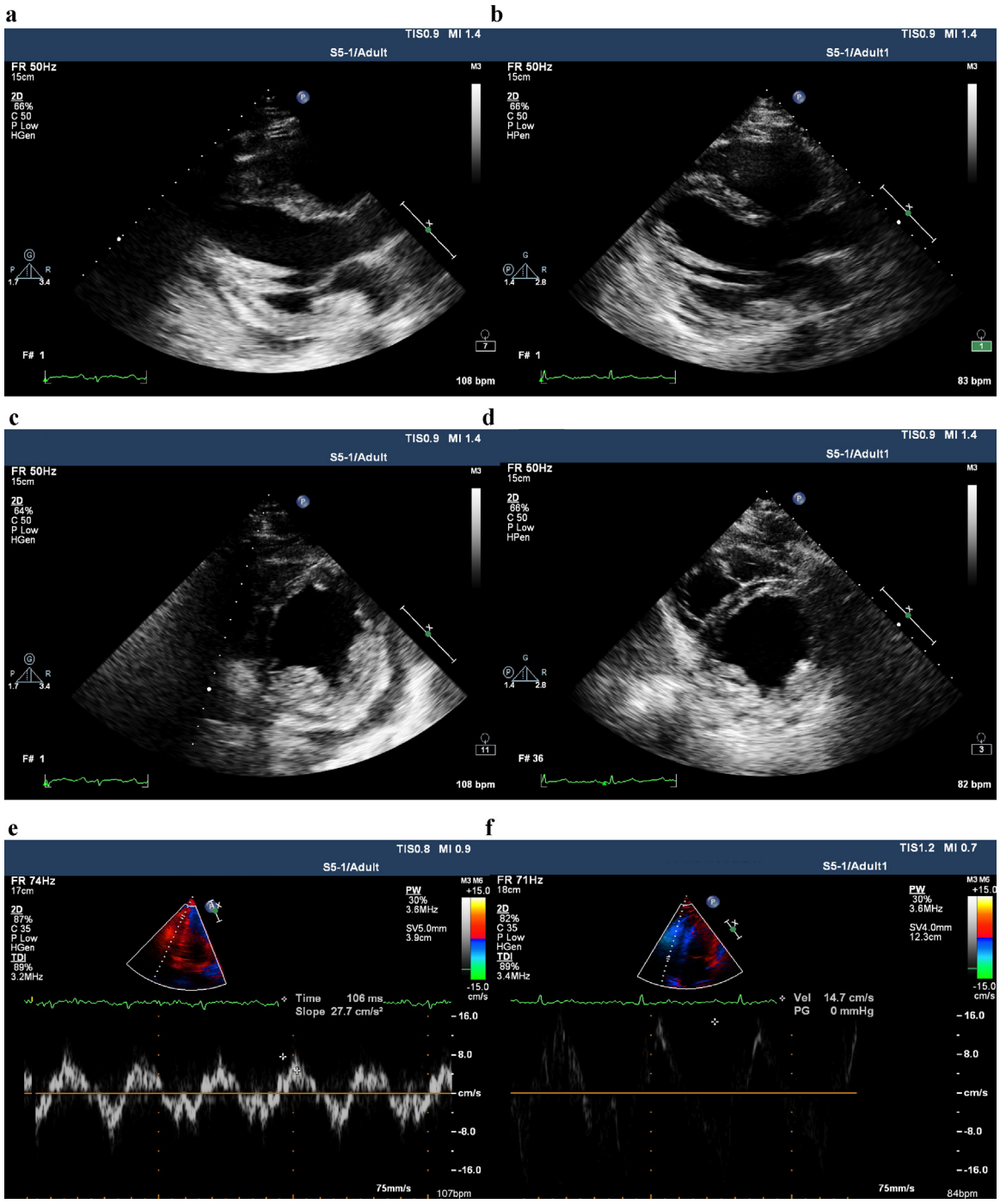

Fig. 1. Transthoracic study on admission (a, c, e) and 5 days after the first cyclophophamide infusion (b, d, f). (a, b) Left parasternal long-axis view, transthoracic echocardiography. Left ventricular hyperechogenicity, mitral annular infiltration and moderate pericardial effusion causing right ventricular protodiastolic compression (a) are attenuated upon treatment (b). (c, d) Left parasternal short-axis view, papillary muscle level, transthoracic echocardiography. Left ventricular and papillary muscle infiltration, moderate pericardial effusion. Endocardial, myocardial, subepicardial, and pericardial involvement can be demonstrated in this view (c). Upon treatment, ongoing hyperechogenicity affecting the subepicardial and subendocardial left ventricular wall – here most prominent within the inferior and inferolateral segments – as well as the papillary muscles probably reflects ongoing fibrosis and may have resulted from previous subclinical myocardial disease. All three facets of the inflammatory response – namely acute/chronic inflammation and healing/fibrosis – may coexist to various degrees (d). (e, f) Tissue Doppler examination. Reduced tricuspid annular systolic velocity (8 cm/s) reflecting abnormal right ventricular systolic function (e) normalizes upon treatment (14 cm/s) (f).

Repeat echocardiogram, 5 days later, demonstrated improved global systolic function (ejection fraction = 50–55%) with residual inferior/inferolateral hypokinesia and slightly less infiltration (Fig. 1b, d and f). Right ventricular function had normalized (tricuspid annular systolic velocity = 14 cm/s). There was a small pericardial effusion with no signs of constriction. Global left ventricular longitudinal (GLS: −16%) and circumferential (GCS: 21%) strain had improved; however, inferior/inferolateral segments still exhibited markedly abnormal deformation parameters probably indicating an ongoing fibrotic process

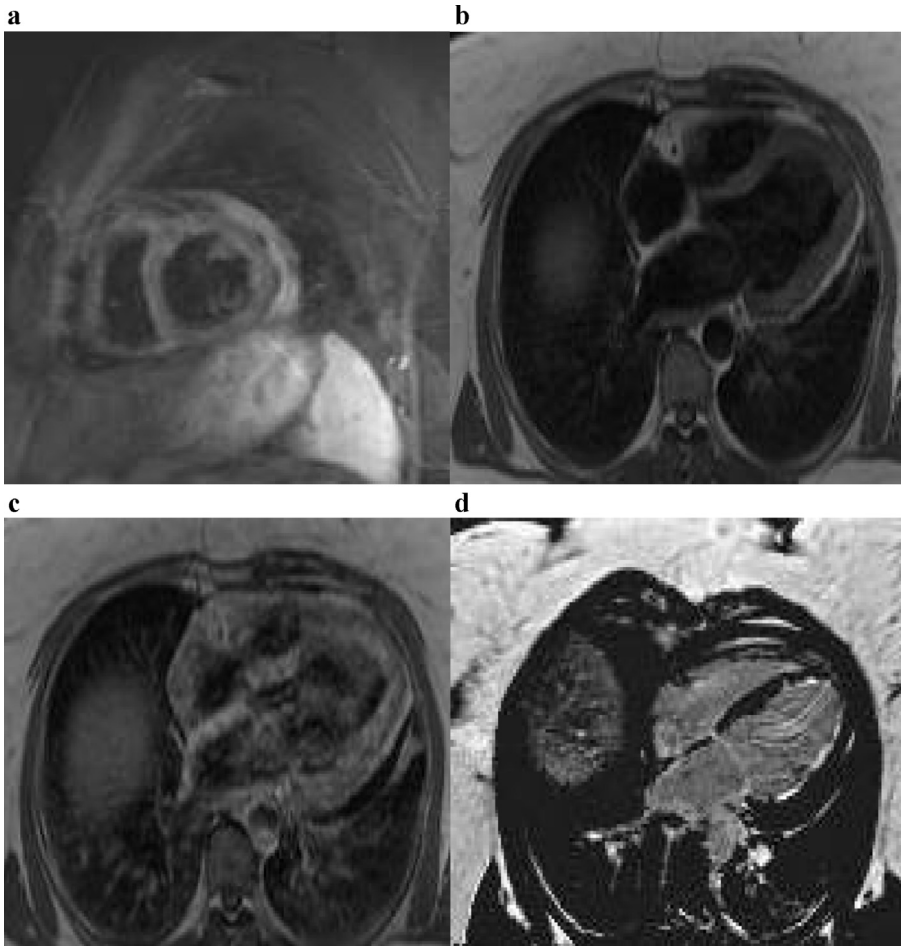

Fig. 2. Cardiac magnetic resonance imaging 15 days after the first cyclophosphamide infusion. Cardiac magnetic resonance examination was performed in a 1.5 T system using short tau inversion recovery (STIR) T2-weighted (T2-W), T1-weighted (T1-W) before and after contrast media injection and late enhanced images (LGE). (a) Electrocardiogram (ECG)-triggered, STIR T2-W sequence was performed in short axis and the signal ratio measured from the region of interest covering the myocardium of the left ventricle (LV) as well as within a skeletal muscle in the same slice. (b, c) ECG-triggered T1-W multislice spin-echo images were obtained in axial orientation with identical parameters before and after an intravenous bolus of 0.1 mmol/kg gadolinium diethylene triamine penta-acetic acid (Gd-DTPA). Measurements after Gd-DTPA were started within 1 min of injection (early T1 = EGE). (d) Immediately after the second set of T1-W images, 0.1 mmol/kg Gd-DTPA was given again and LGE images were taken 15 min later. A steady-state free-precession sequence was used for the evaluation of LV function. Images were analyzed according to previously described protocols [5].

(peak systolic strain −8%, circumferential strain 15%, respectively).

Cardiac magnetic resonance imaging was performed 15 days after the first CYC infusion. Despite the presence of normal biventricular systolic function and dimensions (LV ejection fraction = 61%), all three facets of the inflammatory process namely acute/chronic inflammation and healing were evident to various degrees. More specifically, an increased signal intensity ratio of 2.8 (signal intensity normalized to skeletal muscle in the same slice, normal values < 2) indicative of edema with abnormal early (EGE = 6, normal values < 4) and positive late gadolinium enhancement (LGE) – illustrative of hyperemia/capillary leak and fibrosis respectively – were seen. Importantly, fibrosis was also evident in the right ventricular free wall and apex (Fig. 2d).

The patient is now receiving monthly CYC, small doses of metoprolol and ramipril and is reasonably well. Her global systolic function remains normal and she has no pericardial effusion. She undergoes periodic evaluation with 24-h Holter monitoring based on the findings of extensive fibrosis – right ventricular LGE may be indicative of a particularly arrhythmogenic substrate – which has shown no major abnormality so far.

Discussion

CSS is a necrotizing small vessel vasculitis. Late onset asthma, nasal polyps, and sinusitis are early disease manifestations whereas tissue eosinophilia, pulmonary infiltrations, and multiple organ dysfunction occur later in the disease course. Gastrointestinal and myocardial involvement may lead to life-threatening complications and they usually imply a demise prognosis. The American College of Rheumatology (ACR) diagnostic criteria for CSS include asthma, peripheral eosinophilia (>10% of white blood cells), pulmonary infiltrates, mononeuropathy or polyneuropathy, paranasal sinus abnormality, and histologic evidence of extravascular eosinophil infiltration [1]. The presence of 4/6 ACR criteria establishes the diagnosis.

Cardiac involvement is evident in 40–50% of the CSS cases and carries poor prognosis. It may manifest as eosinophilic myocarditis, pericarditis or tamponade, valvular heart disease, congestive heart failure, or myocardial infarction from epicardial coronary vasculitis. LV thrombi are common. The combination of asthma, eosinophilia, and myocardial/pericardial involvement should alert cardiologists toward the diagnosis of CSS in previously undiagnosed patients. Our patient fulfilled 4 criteria for CSS and based on

her previous history, the diagnosis of CSS with myopericardial involvement could safely be made.

Eosinophils are toxic pro-inflammatory effector cells with a major role in inflammation and tissue damage observed in eosinophil-associated diseases (CSS, eosinophilic leukemia, hypereosinophilic syndrome, Loeffler's endocarditis). Any process associated with hypereosinophilia lasting for several weeks or months may lead to eosinophilic myocarditis. Either primarily or secondarily overproduced, eosinophils contain T-cell derived cytokines and growth factors such as interleukin-3, granulocyte macrophage-colony stimulating factor, and interleukin-5, capable of inducing excessive inflammation, tissue damage, and fibrosis.

Some of the features of myocardial CSS involvement can be evaluated by echocardiography; however, this is not 100% sensitive for detection of subtle changes. Inflammation/edema and fibrosis – perhaps reflecting "healed" inflammation and accounting for diastolic dysfunction and restrictive cardiomyopathy – can coexist but are not always possible to be appropriately classified with traditional echocardiography [2]. Deformation parameters, although not established for diagnostic purposes, may provide useful insight in the characterization of tissue mechanics reflecting histopathological changes of CSS even in subclinical disease. Features such as diminished circumferential strain, reduced LV torsion, and segmental post-systolic shortening may be linked to myocardial infiltration/fibrosis and diastolic dysfunction or features of restrictive cardiomyopathy and enhance the sensitivity of the method for the detection of myocardial involvement in ambiguous cases [3].

Cardiac magnetic resonance imaging is advocated as the gold-standard method to look for preclinical cardiac involvement in CSS patients. This is of major importance since immunosuppression with CYC and high-dose steroids should be promptly instituted in the case of heart – or other major organ – involvement. Cardiac magnetic resonance imaging can assess disease acuity using T2 imaging that provides edema evaluation. Additionally, if 2/3 evaluated parameters are positive (T2, EGE, LGE), this is a proof of myocardial inflammation. Finally, the location and extent of myocardial scar have a prognostic value, even if LV systolic function remains intact. In our case the LGE = 10% of LV extent had a pattern of diffuse subendocardial fibrosis and involved also right ventricle. These findings carry a poor prognosis and also suggest careful evaluation for future arrhythmia development [4].

To conclude, echocardiography, using the current techniques, is a cheap, bedside, widely available tool that can imply the diagnosis in the appropriate clinical context, and also be used for follow-up. However, its sensitivity, even with the use of new echocardiographic techniques is questionable for the diagnosis of subtle disease. At the moment, cardiac magnetic resonance imaging can answer queries about tissue characterization, disease acuity, and prediction in these patients.

Informed consent has been obtained by the patient for publication of this case report and accompanying images.

Conflict of interest

The authors declare that there is no conflict of interest.

References

[1] Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lightfoot Jr RW, McShane DJ, Mills JA, Stevens MB, Wallace SL, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arhritis Rheum 1990;33:1094–100.

[2] Szczeklik W, Miszalski-Jamka T, Mastalerz L, Sokolowska B, Dropinski J, Banys R, Hor KN, Mazur W, Musial J. Multimodality assessment of cardiac involvement in Churg–Strauss Syndrome patients in clinical remission. Circ J 2001; 75:649–55.

[3] Vitarelli A, Capotosto L, Rosato E, Salsano F. Echocardiographic myocardial imaging reveals segmental cardiomyopathy in Churg–Strauss syndrome. Tex Heart Inst J 2010;37:594–7.

[4] Mavrogeni S, Sfikakis PP, Karabela G, Stavropoulos E, Kolovou G, Kitas GD. All roads lead to Rome ventricular tachycardia due to right ventricle involvement in autoimmune and non-autoimmune disease. Int J Cardiol 2014;173:126–7.

[5] Friedrich MG, Strohm O, Schulz-Menger J, Marciniak H, Luft FC, Dietz R. Contrast media-enhanced magnetic resonance imaging visualizes myocardial changes in the course of viral myocarditis. Circulation 1998;97:1802–9.